NIH CLINICAL TRIAL PLANNING GRANT (R34) PROGRAM

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Department of Health and Human Services (DHHS)

PARTICIPATING ORGANIZATIONS:
National Institutes of Health (NIH)
(http://www.nih.gov)

COMPONENTS OF PARTICIPATING ORGANIZATIONS:
National Institute on Aging (NIA)
(http://www.nia.nih.gov/)
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
(http://www.niaaa.nih.gov/)
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
(http://www.niams.nih.gov/)
National Institute of Child Health and Human Development (NICHD)
(http://www.nichd.nih.gov/)
National Center for Complementary and Alternative Medicine (NCCAM)
(http://www.nccam.nih.gov/)
National Institute on Deafness and Other Communication Disorders (NIDCD)
(http://www.nidcd.nih.gov/)
National Institute on Drug Abuse (NIDA)
(http://www.nida.nih.gov/)
National Institute of Neurological Disorders and Stroke (NINDS)
(http://www.ninds.nih.gov/)
Office of Research on Women's Health (ORWH)
(http://www4.od.nih.gov/orwh/index.html)
Office of Behavioral and Social Sciences Research (OBSSR)
(http://obssr.od.nih.gov/)
Office of Rare Diseases (ORD)
(http://rarediseases.info.nih.gov/)
Office of Dietary Supplements (ODS)
(http://dietary-supplements.info.nih.gov/)

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THIS PA CONTAINS THE FOLLOWING INFORMATION

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PURPOSE OF THIS PA

The purpose of the NIH Clinical Trial Planning Grant (R34) is to provide support for the development of a Phase III clinical trial, including the establishment of the research team, the development of tools for data management and oversight of the research, the definition of recruitment strategies, and the finalization of the protocol and other essential elements of the study included in a manual of operations/procedures. The Clinical Trial Planning Grant is not designed for the collection of preliminary data or the conduct of pilot studies to support the rationale for a clinical trial.

An NIH-defined Phase III clinical trial is a broadly based prospective clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments. Often, the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions for disease prevention, prophylaxis, diagnosis or therapy. Community- and other population-based intervention trials also are included.

The planning grant is designed to permit early peer review of the rationale and design of the proposed clinical trial and to provide support for the development of a detailed Manual of Procedures (MOP) including all elements essential to the launching of a trial.

Investigators wishing to apply for an R34 grant should be aware that individual ICs may have specific requirements for this funding mechanism and, therefore, should consult IC staff to determine if an application is appropriate. NIH Offices that participate in this PA

(ORWH, OBSSR, ORD, ODS) are listed but do not have funding authority and must work through an Institute or Center.

RESEARCH OBJECTIVES

Background

At the time of submission, applications requesting support for Phase III clinical trials are expected to provide detailed information regarding the study's rationale, design, analytic techniques, protocols and procedures, facilities and environment, organizational structure, and collaborative arrangements. This information is best conveyed in a well-documented Manual of Procedures (MOP), the development of which typically represents a costly and time-consuming activity. Delay of the trial caused by the need to develop a MOP reduces the time available to carry out the trial itself. The R34 has been established to allow for the planning and organizational activities necessary to implement a Phase III clinical trial to take place well in advance of funding of the actual trial.

Scope

The planning grant is designed to: (1) permit early peer review of the rationale for the proposed clinical trial; (2) permit assessment of the design/protocol of the proposed trial in its current, early form; (3) provide support for the development of a detailed MOP; and (4) support the development of other essential elements of a clinical trial as defined by the individual participating ICs.

Activities supported by the R34 may include, but are not limited to, the following examples:

o developing/finalizing the Manual of Operations; basic elements in the MOP should include identification of the patient population; inclusion and exclusion criteria; adequate plans for recruitment and retention of participants; experimental design and protocols; clear definition of the research hypothesis and outcome measures; quality control/assurance procedures; data management and analytical techniques; sample size estimates with justification; administrative procedures (including regulatory approvals if necessary); collaborative arrangements; duties and responsibilities of study chairperson, clinical sites, coordinating center, and other central resources such as a central laboratory; and monitoring plans to assure patient protection and data integrity;

o finalizing plans for addressing Federal and NIH gender/minority inclusion and human subjects protection requirements;

o establishing collaborative arrangements;

o instituting means to assure standardization of procedures across sites and among staff;

o developing tools needed for data collection and data management;

o developing/finalizing safety and monitoring plans; in the application, do not name individuals for the Data and Safety Monitoring Board (DSMB), but include areas of expertise that will be tapped in forming the DSMB; contact the relevant IC for specific DSMB policies;

o developing plans for any training that may be required to carry out the proposed trial, including, for example, training of data collectors and individuals who will carry out the planned intervention.

Please note that an IC may support any or all of these activities; see http://grants.nih.gov/grants/funding/r34.htm for contact information and specific IC requirements regarding the content and format of a MOP.

The Clinical Trial Planning Grant is not designed for the collection of preliminary data or the conduct of pilot studies to support the rationale for a clinical trial. Consider other funding mechanisms to support pilot or feasibility studies; IC staff should be consulted for guidance.

It is expected that receipt of an R34 grant will lead to the timely submission of an application for support of the full-scale trial, incorporating the elements developed under the planning grant. Prospective applicants should note that funding of a Clinical Trial Planning Grant does not guarantee or imply funding for a subsequent application.

MECHANISM OF SUPPORT

This PA will use the NIH Clinical Trial Planning Grant (R34) award mechanism.
As an applicant, you will be solely responsible for planning, directing, and executing the proposed project.

You may request a project period of one year and a budget for direct costs of up to four $25,000 modules or $100,000 per year.

This PA uses just-in-time concepts. It also uses the modular budgeting format (see http://grants.nih.gov/grants/funding/modular/modular.htm). Specifically, if you are submitting an application with direct costs in each year of $250,000 or less, use the modular format. This program does not require cost sharing as defined in the current NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2001/part_i_1.htm.

Planning Grant support is for new projects only; competing continuation applications will not be accepted.

ELIGIBLE INSTITUTIONS

You may submit (an) application(s) if your institution has any of the following characteristics:

o For-profit or non-profit organizations
o Public or private institutions, such as universities, colleges, hospitals, and laboratories
o Units of State and local governments
o Eligible agencies of the Federal government
o Domestic or foreign institutions/organizations
o Faith-based or community-based organizations

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

SPECIAL REQUIREMENTS

Minimum Application Requirements

Future Clinical Trial:

o Rationale/Significance - Provide the rationale for the future clinical trial, documenting the significance and need to perform the trial. Describe the potential impact of the clinical trial on health care, policy or practice.

o Research Design and Methods - Enough information should be provided to allow reviewers to evaluate how the trial would be conducted.

o Inclusion and Human Subjects Issues – The application must address the availability and population description of the requisite patient population and plans for recruitment

outreach and follow-up. In addition, plans for addressing issues and challenges regarding adherence to the proposed intervention protocol should be included.
Planning Period Activities:

o Justification for the Planning Grant – Explain the need for the planning grant. Describe the anticipated advantages to beginning the proposed RCT after planning period support as contrasted to beginning the trial without such support.

o Investigators - The application must include a description of the leadership and proposed organization of the clinical trial, including proposed clinical sites (letters of commitment are not required at this stage). This includes the ability of the Principal Investigator to bring together the necessary trial network. Describe the mechanism for identification and selection of additional collaborators. Describe the participants in the planning process, their roles in the development of the plan, and their experience in related studies.

o Planning Activities - Specify how the planning period will be used. The application should include the specific aims and rationale for the planning period, and descriptions of the activities to be carried out.

WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues. Because the participating ICs may have specific programmatic interests in their use of the Planning Grant, you are encouraged to contact relevant staff prior to submitting an application. A listing of NIH contacts for the Clinical Trial Planning Grant (R34) program may be found at: http://grants.nih.gov/grants/funding/r34.htm.

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). Applications must have a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. The DUNS number can be obtained by calling (866) 705-5711 or through the web site at http://www.dunandbradstreet.com/. The DUNS number should be entered on line 11 of the face page of the PHS 398 form. The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

The title , "NIH Clinical Trial Planning Grant (R34) Program," and number of the program announcement (PA-04-008) must be typed on line 2 of the face page of the application form and the YES box must be marked

APPLICATION RECEIPT DATES: Applications submitted in response to this program announcement will be accepted at the standard application deadlines, which are available at http://grants.nih.gov/grants/dates.htm. Application deadlines are also indicated in the PHS 398 application kit.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: Applications requesting up to $250,000 per year in direct costs must be submitted in a modular grant format. The modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in $25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at http://grants.nih.gov/grants/funding/phs398/phs398.html includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at http://grants.nih.gov/grants/funding/modular/modular.htm.

For the NIH Clinical Trial Planning Grant (R34), you may request direct costs in $25,000 modules, up to a total direct cost request of $100,000 for one year.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

APPLICATION PROCESSING: Applications must be mailed on or before the receipt dates described at http://grants.nih.gov/grants/funding/submissionschedule.htm. The CSR will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an application already reviewed, but such application must include an Introduction addressing the previous critique.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight weeks.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. An appropriate scientific review group convened in accordance with the standard NIH peer review procedures (http://www.csr.nih.gov/refrev.htm) will evaluate applications for scientific and technical merit. In general, continuity will be maintained between the review of the planning grant application and the review of the eventual application for the proposed clinical trial.

As part of the initial merit review, all applications will:

o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
o Receive a written critique
o Receive a second level review by the appropriate national advisory council or board.

REVIEW CRITERIA

The NIH R34 is designed to support planning activities in preparation for a full-scale Phase III clinical trial. These activities are primarily logistical, conceptual, and/or technical in nature. They do not involve the collection of data typical of research-related activities supported by the traditional NIH research project grant. As such, the evaluation of R34 applications will focus on the justification of or need for the proposed trial along with the appropriateness of the proposed planning activities.

The Future Clinical Trial:

(1) RATIONALE/SIGNIFICANCE

Are the significance and need to perform a future full-scale randomized clinical trial (RCT) adequately justified? Would the results of the proposed trial be likely to affect health care policy or practice?

(2) APPROACH

Are the conceptual framework, design, methods, and analyses, as currently developed, appropriate for the aim of the future RCT?

The reviewers should consider the appropriateness of the intervention(s), selection of endpoints, study population (inclusion/exclusion criteria), randomization schemes, data management, statistical analysis, recruitment and retention plans, and capacity to generalize results.

(3) INVESTIGATORS

Is the investigator appropriately trained and suited to carry out the proposed trial? Is the work proposed appropriate to the experience level of the Principal Investigator and the research team? Is there clear evidence of leadership? Is there evidence documenting the investigators' ability to organize and manage complex projects?

(4) ENVIRONMENT

Does the scientific environment in which the proposed clinical will be carried out contribute to the probability of success? Will the proposed clinical trial take advantage of the unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

The Planning Period Activities:

(1) RATIONALE/SIGNIFICANCE

Is the planning period necessary? Will the activities planned enhance the development of the future clinical trial? Will the proposed planning period address major barriers to the future clinical trial?

(2) APPROACH

Evaluate the adequacy of the activities proposed for the planning period. Will these activities contribute to the likelihood of timely and successful trial implementation? Can these activities be accomplished in the proposed time period? These activities may include, but are not limited to: (a) developing/finalizing the MOP; (b) finalizing plans for addressing gender/minority inclusion and human subjects protection requirements; (c) establishing collaborative arrangements; (d) developing tools needed for data collection and data management; (e) developing/finalizing safety and monitoring plans (applicants are asked not to name individuals for the DSMB but only to include areas of expertise that will be tapped in forming the DSMB); (f) developing plans for Certification Training.

(3) INVESTIGATORS

Is the investigator appropriately trained and suited to carry out the proposed planning activities? Is the work proposed appropriate to the experience level of the Principal Investigator and the research team? Is there clear evidence of leadership? Is there evidence documenting the investigators' ability to plan, organize, and manage complex projects?

(4) ENVIRONMENT/ORGANIZATION

Does the scientific environment in which the planning activities will take place contribute to the probability of success? Are there adequate plans for the development of an effective organizational structure for carrying out the proposed trial? Are there adequate plans for the development of an essential committee structure, e.g., Steering, Executive, Planning, Data and Safety Committees? Does the application appropriately address issues such as the flow of information to and from the Coordinating Center, to the enrolling centers, and to the appropriate committees?

ADDITIONAL CONSIDERATIONS

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed activities.

AWARD CRITERIA

Applications submitted in response to a PA will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

o Scientific merit of the proposed project as determined by peer review
o Availability of funds
o Relevance to program priorities

REQUIRED FEDERAL CITATIONS

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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Department of Health and Human Services

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